REMARKS

I. PROSECUTION HISTORY

Applicants elected claims 26, 30, and 31 (Group VII) with traverse in response to a restriction requirement mailed May 17, 2002, in which the Office alleged that the claims as filed were directed to twelve distinct inventions. In an action mailed December 3, 2002, the Office maintained the restriction and rejected the elected claims 26, 30 and 31 on various grounds, and additionally presented objections relating to priority and the previously submitted Information Disclosure Statement. In a final action mailed August 27, 2003, the Office rejected claims 26, 30, 31, 38 and 39 on various grounds, and withdrew claims 40-43 for allegedly being directed to a non-elected invention, claims 1-14, 27-29, and 32-37 having been earlier withdrawn.

Applicants responded to the final action on October 27, 2003, and concurrently filed a petition for withdraw of finality. On January 22, 2004, the Office issued a Decision on Petition, which withdrew the finality of the August 27, 2003 Office action and rejoined claims 40-43. The Office also stated that the present application was being forwarded to the Examiner for full consideration of Applicants' June and October 2003 amendment and responses, and the elected invention as clarified in the Decision on Petition.

In a non-final action mailed March 9, 2004, the Office withdrew the August 27, 2003 action and rejected claims 26, 30, 31 and 38-43 under 35 U.S.C. § 112. Applicants thank Examiner Li and her supervisor James Housel for their assistance during a phone interview on April 20, 2004.

Upon entrance of the present amendment, claims 26, 30, 31, and 38, 39, and 42-54 will be pending and, Applicants submit, in condition for allowance.

II. EXPLANATION OF AMENDMENTS

A. In the Specification

The amendment to the specification updates the priority claim paragraph in view of the issuance of one of the priority applications. This paragraph was previously amended as part of a preliminary amendment filed March 22, 2000. U.S. Patent Application No. 09/067,447, another priority application, has been allowed and is scheduled to issue May 18, 2004 as U.S. Pat. No. 6,737,513.

B. In the Claims

The amendment to the claims introduces no new matter, and finds support throughout the specification.

Withdrawn claims have been canceled in order to put the application in condition for allowance. Claims 40 and 41 have also been canceled without prejudice and to expedite prosecution. Claims 26, 30, 42, and 43 have been amended in a manner consistent with the suggestion presented during the April 20, 2004 interview. Claim 31 has been amended to correct typographical errors and finds support, *e.g.*, in the specification at page 14, lines 15-18. The amendment to claim 38 finds support, *e.g.*, in claim 39. New claims 44-46 refer to TARC, but are otherwise analogous to claims 31, 38, and 39. New claim 47 finds support in claim 38 and in the specification at page 14, lines 26-28, page 72, lines 15-26, page 78, lines 1-15, and page 102, lines 24-28. New claim 52 finds support, *e.g.*, at page 105, line 28, to page 106, line 7. New claims 48, 50, and 53 find support, *e.g.*, at page 6, lines 25-29, page 83, lines 7-17, and page 86, lines 16-21. New claims 49, 51, and 54 find support, *e.g.*, at page 14, lines 15-18, page 25, lines 27-29. New claims 44-54 fall within the scope of Group VII, the elected group, consistent with the Office's January 21, 2004 decision on Applicants' petition. *See* Decision on Petition, final paragraph at page 4, and first paragraph of page 5.

Applicants reserve the right to pursue, in this or related applications, claims directed to any unclaimed subject matter whether originally claimed, later claimed, or not previously claimed.

III. THE CLAIMS ARE ENABLED BY THE SPECIFICATION AS FILED

In paragraph 2 of the Office action, the Office rejected claims 26, 30-31, and 38-43 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement in respect to any or all MDC or TARC antagonist for treating any or all allergic reaction in a subject. Applicants respectfully traverse, and believe the rejection to be moot with the entrance of the current amendment in view of Applicants' interview with the examiner and her supervisor. In that interview, the Office indicated that the claims would be allowable in respect to antibodies and polypeptides comprising antigen-binding fragments of the same. Moreover, no undue experimentation would be necessary to practice the invention for the reasons outlined below.

The antagonists recited in the pending claims are antibody substances that bind MDC or TARC; the claims do not require that the antibody substances have any direct or indirect interaction with CCR4 in the palliation of allergic reactions.[1] Accordingly, earlier speculation that CCR4 may play a role in such therapies and subsequent research suggesting that CCR4 is not so involved does not detract in any way from the enabling disclosure of the specification as filed.

In their June 2003 response to the first Office action, Applicants provided as evidence of their enabling disclosure three journal articles reporting successful palliation of allergic reactions with either MDC antagonists or TARC antagonists using techniques consistent with the protocols provided in the specification. Those three journal articles were provided as Exhibits C, D, and E, and Applicants respectfully request that the Office reference those exhibits while considering the following remarks.

A. Published Studies Demonstrate That The Specification Is Enabling

Tissues of allergic inflammation are infiltrated by T_H2 cells and eosinophils. As discussed in the specification, agents that interfere with the interactions of TARC or MDC with T_H2 cells and eosinophils have therapeutic indications for reducing allergic inflammatory responses. The specification specifically contemplates the use of agents to treat allergic inflammatory disorders, *e.g.*, asthma, conditions characterized by eosinophil accumulation. *See* specification, page 105, line 18, to page 106, line 7.

Example 33, beginning on page 107 of the specification describes an antigen-induced asthma/allergy model. A mammalian subject, *e.g.*, a mouse, is given a substance such as ovalbumin to challenge the subject's immune system and elicit an allergic reaction. A known or putative MDC antagonist compound is then administered to the subject, and the subject is monitored to see if the compound is capable of palliating the allergic reaction. One way of assessing this capability is looking for a reduction in eosinophils and/or neutrophils in the lavage fluid (fluid taken from the respiratory tract, *e.g.*, lungs, of the subject) in experimental subjects versus control subjects. These techniques are similarly applicable to TARC antagonists.

Since the present application was filed, a number of groups have published studies that demonstrate that the invention works as described in the application.

[1] However, the lack of such a requirement does not exclude CCR4 from playing a role in palliation.

1. Gonzalo Demonstrates the Enabling Disclosure of the Present Application.

Gonzalo, *et al.*, *Mouse Monocyte-Dervived Chemokine is Involved in Airway Hyperactivity and Lung Inflammation*, J. Immunol., 163: 403-411 (1999) (hereinafter Gonzalo or Appendix C) is attached as Appendix C.[2] Gonzalo used an anti-MDC antibody to suppress eosinophil recruitment in a mouse model of allergy. Gonzalo generated the allergic response with ovalbumin (OVA) (*see* page 404, first column), the same allergen taught in Example 33. Gonzalo's experimental mice were pretreated with the anti-MDC antibody, consistent with Example 33 (page 107, lines 26-29). A substantial reduction of eosinophils (page 407, second column, figure 4) occurred in the experimental mice. The efficacy of anti-MDC antibodies in decreasing the number of eosinophils, as taught in the present application (page 108, lines 1 and 2), is demonstrated by comparing the results in figure 4B for Gonzalo's control (Rb Ig) mice that received a non-MDC antibody and experimental mice that received an anti-mMDC antibody This efficacy of anti-MDC antibodies is further demonstrated by the specific reduction of eosinophils in the lung interstitium, an area of the lung affected by the allergen, in figure 5. (*See* figures 4 and 5 on page 409, and discussion of the same.)

Accordingly, Gonzalo demonstrates that the invention as disclosed in the present application can be practiced effectively to palliate an allergic reaction.

2. Lloyd Demonstrates the Enabling Disclosure of the Present Application.

Lloyd, *et al.*, *CC Chemokine Receptor (CCR3)/Eotaxin is Followed by CCR4/Monocyte-Derived Chemokine in Mediating Pulmonary T Helper Lymphocyte Type 2 Recruitment after Serial Antigen Challenge In Vivo*, J. Exp. Med., 191: 265-73 (2000) (hereinafter Lloyd or Appendix D) describes a study similar to that in Gonzalo with ovalbumin-challenged mice treated with anti-MDC antibodies, *i.e.*, "neutralizing Abs." (*See* page 269, column 2.) Inspection of figure 4A of Lloyd shows that anti-MDC antibodies decreased eosinophil migration by approximately two-thirds compared to control subjects. (*See* page 272 for figure 4, and page 270 for discussion thereof.) Like the results in Gonzalo, these results also comport with those stated in Example 33.

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[2] "Monocyte-Derived Chemokine" as used in Gonzalo is the same chemokine as "Macrophage-Derived Chemokine" of the present application.

Accordingly, Lloyd demonstrates that the invention as disclosed in the present application can be practiced effectively to palliate an allergic reaction.

3. Kawasaki Demonstrates the Enabling Disclosure of the Present Application.

Kawasaki, *et al.*, *Intervention of Thymus and Activation-Regulated Chemokine Attenuates the Development of Allergic Airway Inflammation and Hyperresponseiveness in Mice*, J. Immunol., 166: 2055-2062 (2001) (hereinafter Kawasaki or Appendix E) discloses an experimental study involving a mouse allergy model, in which anti-TARC antibodies are used to cause a dramatic decrease in the number of eosinophils. Kawasaki describes the methods used for the study including the use of ovalbumin as the allergen, and application of antibody prior to induction with the allergen (page 2056, column 1), which mirror the methods presented in Example 33. Kawasaki states: "Treatment with anti-TARC Ab strikingly decreased the total cell number and the number of eosinophils as well as lymphocytes recovered in the lavage fluid compared with those in the group treated with control Ab (Fig. 4)." (Page 2058 and in figure 4 on page 2059.) A decrease in neutrophils is also reported (*see* figure 4) in agreement with Example 33 (specification, page 108, lines 1-2).

Accordingly, Kawasaki demonstrates that the invention using TARC antagonists can be practiced effectively to palliate an allergic reaction, as disclosed in the present application.

4. Summary

The published studies discussed herein demonstrate that the claimed invention can be practiced successfully as described in the specification. Accordingly, the rejection of the claims under 35 U.S.C. § 112, first paragraph should be withdrawn.

B. The Level Of Skill In The Art, The Examples And The Amount Of Guidance Provided Indicate That The Specification Enables One Of Skill To Perform The Full Scope Of The Claimed Invention

The Examiner characterized the level of skill in the art as "high." The greater the knowledge in the art about the field of the invention, the less information needs to be explicitly stated in the specification. *See* M.P.E.P. § 2164.03. The specification of the present application provides detailed guidance regarding specific inhibitors, *see, e.g.*, page 12 of the specification, and to methods of using a MDC antagonist to palliate an allergic reaction

in a mammalian host, *see, e.g.*, Example 33. The detailed instructions in the specification, combined with the high level of skill in the art, means that the specification is enabling.

The Examiner further characterized the Applicants' teaching as limited and also alleged that the claims are too broad in respect to a method of treating an allergic reaction by using any or all MDC antagonists or TARC antagonists. The Applicants respectfully disagree.

The presence or absence of an example is not determinative on the issue of enablement, and an applicant need not describe all actual embodiments in order to have an enabling disclosure. *See* M.P.E.P. § 2164.02. Example 33, beginning on page 107 of the specification demonstrates how MDC antagonists and TARC antagonists can be tested and used to palliate an allergic reaction. Antibodies 252Y and 252Z, described in Examples 18, as well as other antibody substances, may be used according to the teachings of Example 33.

Accordingly, the rejection of the claims under 35 U.S.C. § 112, first paragraph, should be withdrawn. Similarly, any rejection of new claims 44-54 under 35 U.S.C. § 112, first paragraph, would also be improper.

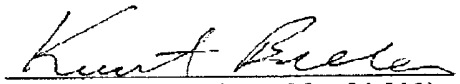
SUMMARY

Applicants respectfully request prompt reconsideration of the pending claims. The claims are believed to be in condition for allowance in view of the foregoing amendments and remarks. Withdrawal of the rejections and allowance of the claims are respectfully solicited.

The Examiner is invited to contact the undersigned at the telephone number listed below in order to discuss any remaining issues or matters of form that will move this case to allowance.

Respectfully submitted,

MARSHALL, GERSTEIN & BORUN LLP

By 

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